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Supplemental Material

Air Pollution from Road Traffic and Systemic Inflammation in Adults: A Cross-Sectional Analysis in the European ESCAPE Project

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Cohort descriptions

The National FINRISK Study has been established in 1972; randomly selected representative population samples are recruited from different parts of Finland every five years (Vartiainen et al. 2010). For this study, three cross-sectional population surveys (1997, 2002, and 2007) and two study areas (cities of Helsinki/Vantaa and Turku/Loimaa region) were used. The KORA study is conducted within the framework of the Cooperative Health Research in the Region of Augsburg, and consists of four cross-sectional, population-representative surveys (Holle et al. 2005). ESCAPE includes two of the surveys, conducted in 1994-1995 and 1999-2001 in the city of Augsburg and two adjacent rural counties. The Heinz Nixdorf Recall study is an ongoing population-based, prospective cardiovascular cohort study that started in 2000, and includes 4,814 randomly selected participants from three large adjacent German cities (Essen, Mülheim/Ruhr, Bochum) (Schmermund et al. 2002). Health data from the baseline examination of the cohort (2000–2003) were used for the current analyses. For the SAPALDIA study, a random population sample across 8 geographic areas (Aarau, Basel, Davos, Geneva, Lugano, Montana, Payerne and Wald) was obtained in 1991 (Ackermann-Liebrich et al. 2005). For the current analyses, data of the 2002 follow-up (when biospecimens for CRP analyses were collected) from Basel, Lugano and Geneva are used. TwinGene is a substudy of SALT (Lichtenstein et al. 2006), which is based on a telephone interview 1998-2002, involving twins from the Swedish National Twin Registry (http://ki.se/en/research/the-swedish-twin-registry). In TwinGene, twins born before 1958 were contacted in the years 2004-2008 for the collection of biological samples. In the 60-year-olds cohort study (Wandell et al. 2007), a random sample of every third man and woman born between 1 July 1937 and 30 June 1938, and living in

Stockholm County, was invited to participation in a thorough health screening between August 1997 to March 1999. In total 4234 persons participated.

Biochemical measurements

In KORA, plasma CRP concentrations were measured with a high-sensitivity immunoradiometric assay from the blood samples taken during the 1994-1995 baseline visits (Hutchinson et al. 2000). Dade Behring N Latex High Sensitivity CRP mono assay on a Behring Nephelometer II (BN II) analyser was used for the blood samples of the later baseline visits (2000–2001). Fibrinogen plasma concentrations were determined by immunonephelometry on a BN II analyzer (Siemens, Marburg, Germany).

In HNR, high-sensitive CRP was measured with an automated nephelometer (BN II, Dade-Behring Inc, Deerfield, USA). Fibrinogen in plasma was measured with a Clauss method using an automated BCS-Analyzer (Dade-Behring Inc, Deerfield, USA). All analyses were performed in the central laboratory of the University Hospital of Essen.

In SAPALDIA, high-sensitive CRP serum levels were measured using Hitachi Modular Autoanalyser (Rotkreuz, Switzerland) and a latex-enhanced immunoturbidimetric assay (Roche Diagnostics, Mannheim, Germany).

In FINRISK, high-sensitive CRP was analyzed from the blood samples of the baseline visits of 1997 and 2007 using a latex immunoassay (Sentinel Diagnostics, Milan, Italy) with Architect c8000 analyser (Abbot Laboratories, Abbott Park, Illinois, US). Concerning the 2002 baseline visits, equipment by Orion Diagnostica (Espoo, Finland) was used for the immunoturbidometric assay coupled with the Optima analyser (Thermo Elektron, Waltham, MA, US). Fibrinogen was measured with the Clauss method using IL Test Fibrinogen-C kit and ACL300R equipment (Instrumentation Laboratory, Milan, Italy).

In TwinGene, high-sensitive CRP was determined using Synchron LX systems (Beckman Coulter, Brea, California, US). Fibrinogen was measured in the cohort of 60-year-olds by a functional spectrophotometric test (Boehringer Mannheim, Germany).

Table S1. Associations of air pollution and indices of traffic intensity with C-reactive protein and fibrinogen in sensitivity analyses. Main models run adjusting for traffic noise levels, use of antihypertensive medication or statins, and excluding persons moving within 2 years before blood sampling. Effect estimates calculated for a change of 5 μg/m^3 in $PM_{2.5}$ and PM_{coarse}, 10 μg/m^3 in PM_{10} and NO_2, 20 μg/m^3 in NO_x, and $1x10^{-5}$/m in $PM_{2.5}$ absorbance.

	Traffic noise		Moving history		Antihypertensives		Statins	
Exposures	**% Diff[a] (95% CI)**	**P_{heter}[b]**	**% Diff[a] (95% CI)**	**P_{heter}[b]**	**% Diff[a] (95% CI)**	**P_{heter}[b]**	**% Diff[a] (95% CI)**	**P_{heter}[b]**
CRP								
$PM_{2.5}$	0.1 (-12.3, 14.3)	0.02	4.1 (-3.1, 11.8)	0.43	2.5 (-6.3, 12.0)	0.13	2.5 (-6.7, 12.7)	0.10
PM_{10}	0.3 (-5.4, 6.2)	0.74	1.3 (-4.2, 7.1)	0.88	0.7 (-4.3, 6.0)	0.92	0.9 (-4.2, 6.2)	0.92
PM_{coarse}	3.3 (-1.3, 8.1)	0.40	3.3 (-0.8, 7.6)	0.65	2.2 (-1.5, 5.9)	0.66	2.1 (-1.5, 5.9)	0.66
$PM_{2.5}$ absorbance	-0.9 (-7.2, 5.8)	0.50	1.7 (-4.7, 8.7)	0.85	0.2 (-5.5, 6.2)	0.85	0.7 (-5.1, 6.8)	0.81
NO_2	1.8 (-1.5, 5.3)	0.62	1.3 (-2.0, 4.7)	0.48	1.8 (-1.1, 4.9)	0.83	1.7 (-1.3, 4.7)	0.83
NO_x	3.4* (0.2, 6.7)	0.98	2.3 (-1.0, 5.8)	0.91	2.9* (0.0, 5.9)	0.99	2.5** (-0.4, 5.4)	0.99
Traffic intensity at the nearest road (vehicles/day)								
<1,000	Ref.		Ref.		Ref.		Ref.	
1,000-5,000	-1.5 (-6.4, 3.7)	0.80	-2.5 (-7.7, 2.9)	0.59	-1.7 (-6.3, 3.2)	0.62	-2.1 (-6.7, 2.7)	0.81
5,000-10,000	8.2* (1.0, 15.9)	0.99	5.1 (-2.3, 13.2)	0.54	2.8 (-6.9, 13.6)	0.28	4.5 (-2.0, 11.6)	0.58
>10,000	11.9* (3.4, 21.2)	0.75	9.9* (1.1, 19.5)	0.64	10.3* (2.4, 18.7)	0.98	9.9* (2.2, 18.3)	0.84
Traffic load within 100 m on major roads (vehicles/day*m)								
<500,000	Ref.		Ref.		Ref.		Ref.	
500,000-1,500,000	1.7 (-6.1, 10.2)	0.21	3.5 (-1.5, 8.8)	0.88	1.0 (-3.4, 5.7)	0.56	1.1 (-3.4, 5.8)	0.54
1,500,000-3,000,000	2.8 (-2.5, 8.4)	0.74	1.7 (-3.8, 7.4)	0.68	1.6 (-3.2, 6.6)	0.91	1.8 (-3.0, 6.9)	0.68
>3,000,000	2.5 (-4.1, 9.5)	0.32	2.8 (-4.3, 10.5)	0.27	2.7 (-4.0, 9.9)	0.21	1.9 (-4.3, 8.5)	0.27
Fibrinogen								
$PM_{2.5}$	0.0 (-1.9, 1.9)	0.63	0.2 (-1.4, 1.9)	0.60	0.1 (-1.4, 1.7)	0.36	-0.0 (-1.6, 1.6)	0.91
PM_{10}	0.2 (-1.3, 1.6)	0.44	-0.1 (-1.7, 1.5)	0.11	-0.1 (-1.5, 1.4)	0.24	-0.1 (-1.6, 1.3)	0.25
PM_{coarse}	-0.3 (-1.5, 0.9)	0.64	-0.1 (-1.5, 1.2)	0.13	-0.3 (-1.2, 0.7)	0.36	-0.3 (-1.2, 0.5)	0.39
$PM_{2.5}$ absorbance	-0.3 (-2.0, 1.4)	0.65	-0.0 (-2.3, 2.3)	0.23	0.0 (-1.4, 1.5)	0.49	-0.0 (-1.5, 1.4)	0.52
NO_2	0.3 (-1.4, 2.0)	0.10	0.3 (-1.1, 1.7)	0.04	0.4 (-0.7, 1.5)	0.11	0.3 (-0.8, 1.4)	0.12
NO_x	0.5 (-0.8, 1.8)	0.18	0.4 (-0.6, 1.5)	0.16	0.5 (-0.5, 1.4)	0.19	0.4 (-0.5, 1.3)	0.24

	Traffic noise		Moving history		Antihypertensives		Statins	
Exposures	**% Diff[a] (95% CI)**	**P_{heter}[b]**	**% Diff[a] (95% CI)**	**P_{heter}[b]**	**% Diff[a] (95% CI)**	**P_{heter}[b]**	**% Diff[a] (95% CI)**	**P_{heter}[b]**
Traffic intensity at the nearest road (vehicles/day)								
<1,000	Ref.		Ref.		Ref.		Ref.	
1,000-5,000	0.5 (-1.7, 2.6)	0.21	0.2 (-1.5, 1.8)	0.29	0.0 (-1.2, 1.2)	0.46	0.1 (-1.1, 1.3)	0.47
5,000-10,000	1.6** (-0.3, 3.5)	0.92	1.9* (0.1, 3.6)	0.98	1.6** (-0.1, 3.4)	0.89	1.7 (0.0, 3.5)	0.96
>10,000	0.9 (-1.2, 3.0)	0.61	0.8 (-1.1, 2.8)	0.74	0.6 (-1.2, 2.5)	0.73	0.6 (-1.3, 2.5)	0.72
Traffic load within 100 m on major roads (vehicles/day*m)								
<500,000	Ref.		Ref.		Ref.		Ref.	
500,000-1,500,000	0.2 (-1.0, 1.3)	0.42	0.3 (-0.8, 1.4)	0.52	0.0 (-1.1, 1.1)	0.48	0.1 (-1.0, 1.3)	0.33
1,500,000-3,000,000	0.9 (-0.4, 2.3)	0.63	1.0 (-0.3, 2.3)	0.95	0.7 (-0.5, 1.9)	0.89	0.8 (-0.5, 2.0)	0.88
>3,000,000	1.0 (-0.9, 2.9)	0.33	1.2 (-0.3, 2.7)	0.64	1.0 (-0.4, 2.4)	0.68	1.0 (-0.4, 2.4)	0.62

Main models run adjusting for traffic noise levels, use of antihypertensive medication or statins, and excluding persons moving within 2 years before blood sampling. Effect estimates calculated for a change of 5 $\mu g/m^3$ in $PM_{2.5}$ and PM_{coarse}, 10 $\mu g/m^3$ in PM_{10} and NO_2, 20 $\mu g/m^3$ in NO_x, and $1x10^{-5}/m$ in $PM_{2.5}$ absorbance.

[a]Percent difference. [b]p-value for heterogeneity.

*Effect estimates with p-values <0.05. **Effect estimates with p-values <0.1.

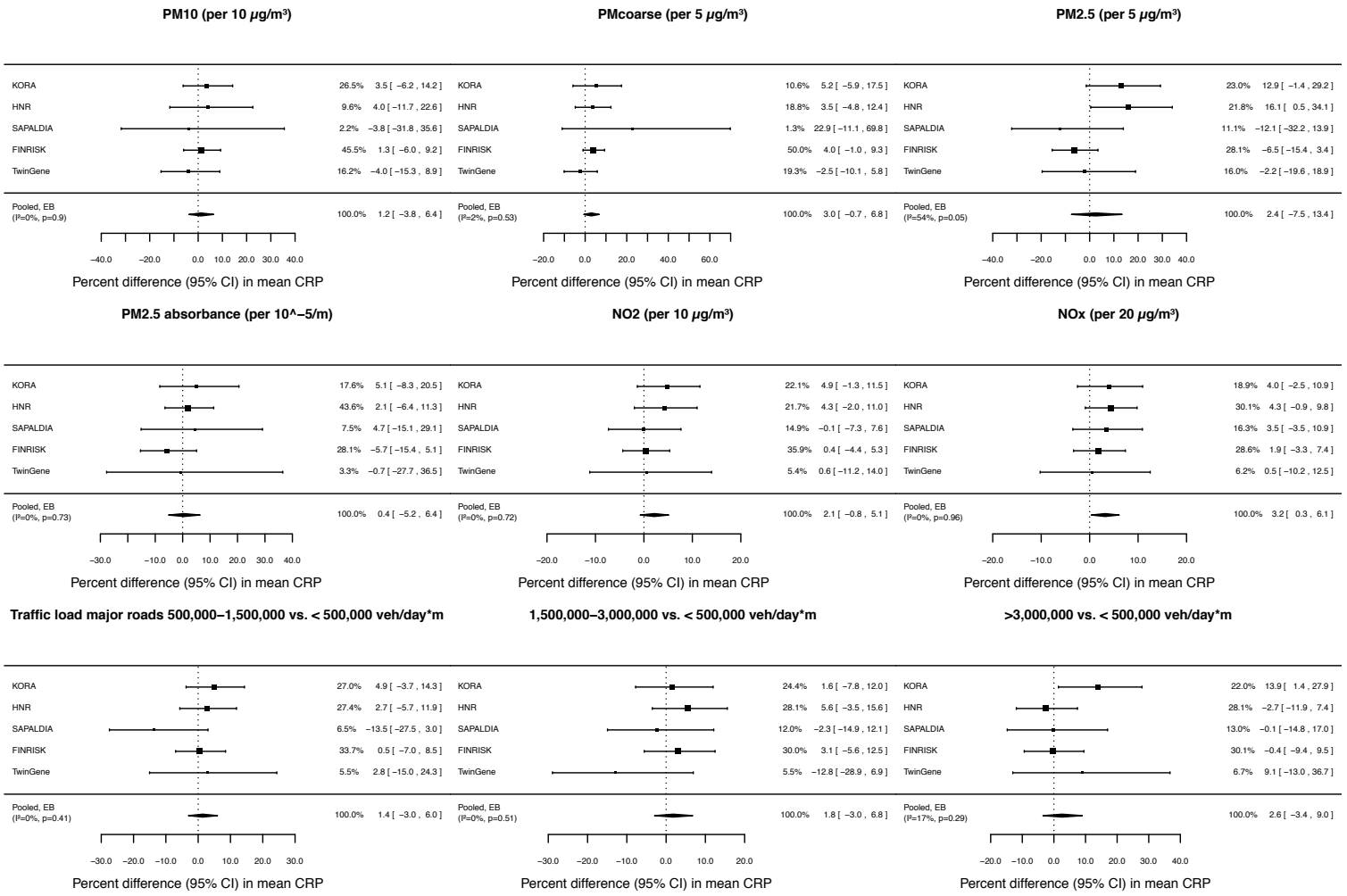

Figure S1. Cohort−specific and pooled exposure effects on CRP (main model). The size of the box indicating point estimate indicates the weight of the individual cohort on results; error bars represent 95% CIs.

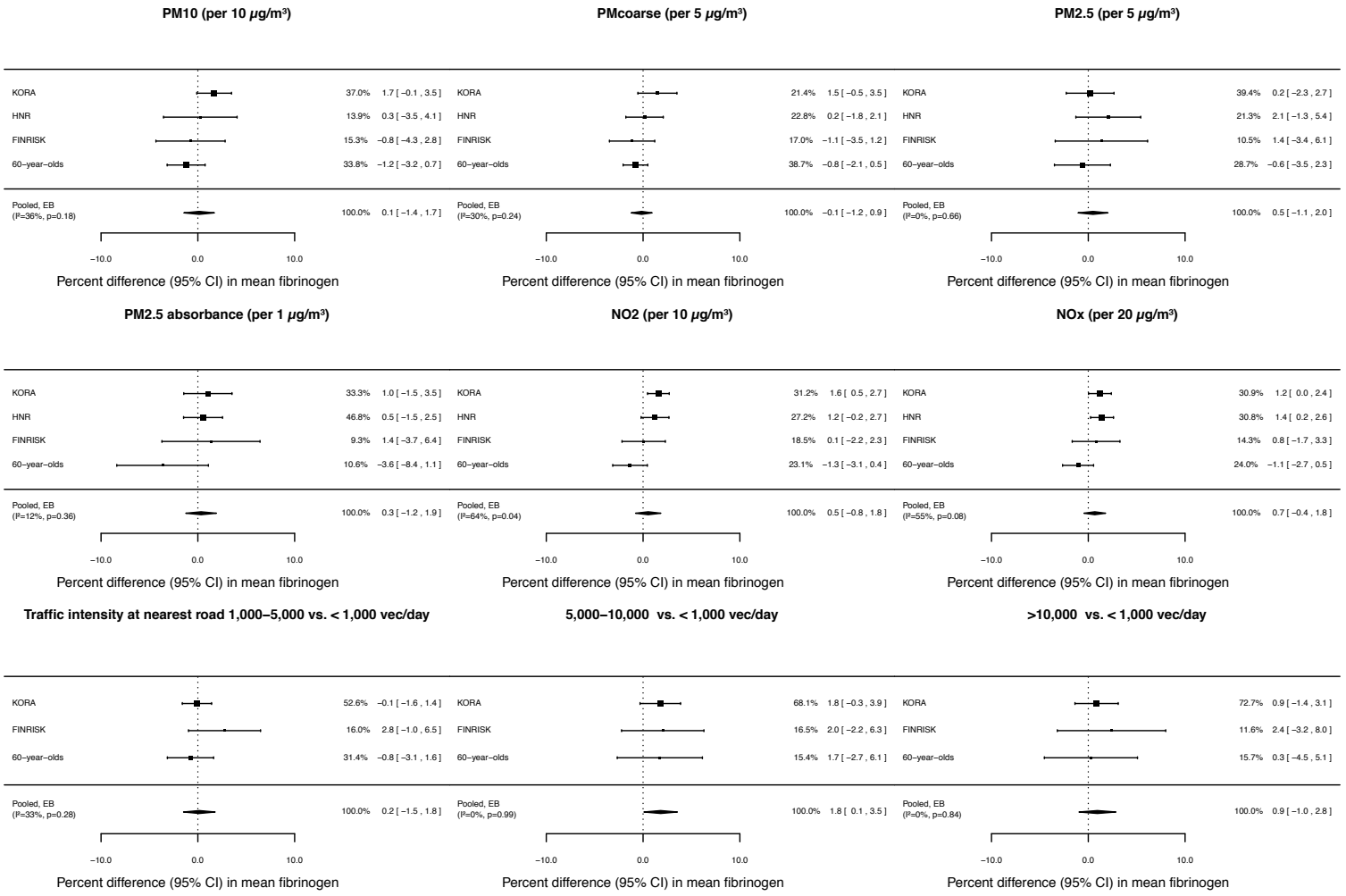

Figure S2. Cohort−specific and pooled exposure effects on fibrinogen (main model). The size of the box indicating point estimate indicates the weight of the individual cohort on results; error bars represent 95% CIs.

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